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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/825,242	04/02/2001	Stephen Eisenberg	019496-001810US	2688

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EXAMINER

BRUSCA, JOHN S

ART UNIT PAPER NUMBER

1631

DATE MAILED: 10/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

### Application No.

09/825,242

### Applicant(s)

EISENBERG ET AL.

### Examiner

John S. Brusca

### Art Unit

1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 07 September 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 35,37,38,40-43,48,49,52 and 53 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 35,37,38,40,42,43,48,49 and 53 is/are rejected.
- 7) ☒ Claim(s) 41 and 52 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 April 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____  |

Art Unit: 1631

## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 112***

1. The rejection of claims 35, 37-43, 48, 49, and 52 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention in the Office action mailed 02 July 2004 is withdrawn in view of the amendment to claims 35, 42, 43, 48, and 49, and the cancellation of claim 39 in the amendment filed 07 September 2004.

### ***Claim Rejections - 35 USC § 103***

2. The rejection of claim 53 under 35 U.S.C. 103(a) as being unpatentable over Desjarlais et al. in the Office action mailed 02 July 2004 is withdrawn in view of the amendment to claim 53 to recite "precharacterized zinc finger proteins" in the amendment filed 07 September 2004.

3. The rejection of claims 35, 37, 38, 40, 42, 43, 48, 49, and 53 under 35 U.S.C. 103(a) as being unpatentable over Choo et al. (1994b) in view of Choo et al. (1994a) in the Office action mailed 02 July 2004 is withdrawn in view of the amendments to claims 35, 42, 43, 48, 49, and 53, and the recitation in claim 37 of conservation of correspondence between positions of zinc fingers in the database and the encoded protein or protein made by the method.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

Art Unit: 1631

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 35, 40, 48, 49, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choo et al. (1994b) (Nature Vol. 372, pages 642-645, reference DB in the information disclosure statement filed 02 April 2001) in view of Choo et al. (1994a) (Proc. Natl. Acad. Sci. USA Vol. 91, pages 11163-11167, reference DD in the information disclosure statement filed 02 April 2001) in view of Corbi et al.

Art Unit: 1631

The claims are drawn to a method of making a zinc finger protein or a polynucleotide encoding a zinc finger protein comprising three zinc fingers that binds to a target site by using a database that comprises a plurality of precharacterized zinc finger protein sequences in which the zinc finger domains are correlated with their respective DNA binding target. The database comprises a zinc finger protein that has a third finger that is different from the third finger of at least one other protein in the database. In some embodiments the claims are drawn to computers or computer programs that execute the method, or a computer mediated method.

Choo et al. (1994b) shows a method of designing a zinc finger protein that binds to a BCR-ABL recombined oncogene target site. Choo et al. (1994b) shows on pages 642-643 that each triplet of the intended binding site (shown in figure 1) was used to screen a randomized zinc finger library made by the method of Choo et al. (1994a). Selected zinc fingers that bound a desired triplet were combined into a set of three finger zinc finger proteins shown in figure 2 and further screened to select the zinc finger protein that bound the intended binding site. One zinc finger designated 1A-2A-3B was selected for expression. The expressed zinc finger protein bound the intended binding site as shown in figure 3. Choo et al. (1994b) does not explicitly show that the randomized library of zinc finger proteins consists of three finger zinc finger proteins, and further does not show the extent of precharacterization of the zinc finger proteins in the randomized zinc finger library or a database of the randomized zinc finger library. Choo et al. (1994b) does not show a computer-mediated method or computers or programs that execute the method. Choo et al. (1994b) does not show a database comprising a zinc finger protein that has a third finger that is different from the third finger of at least one other protein in the database.

Art Unit: 1631

Choo et al. (1994a) shows on pages 11163-11164 a phage library comprising zinc finger genes in which the middle of three fingers is randomized. Choo et al. (1994a) shows on pages 11164-11166 that the library can be used to screen for members that bind the middle triplet of choice of a polynucleotide binding target. Choo et al. (1994a) shows in figure 1 the three fingers and three alternative polynucleotide binding targets. Choo et al. (1994a) shows in figure 2 a database of selected and characterized library members. Choo et al. (1994a) discusses the amino acid sequence and putative secondary structures of the binding region of the selected library members.

Corbi et al. shows a zinc finger gene and protein termed Mago in figures 1-2. The protein has three fingers. Corbi et al. shows in figure 3 the sequence of the target binding site recognized by the zinc finger protein. The third finger has a different sequence than that of the ZIF268 third finger, which appears in the database of Choo et al. (1994a).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to precharacterize the selected random library members of Choo et al. (1994b) to any desired extent to aid in further analysis of selected library members because Choo et al. (1994a) shows such analysis in figure 2 and pages 11164-11167. It would have been further obvious to record such characterizations in a database as shown in Choo et al. (1994a) figure 2. It would have been further obvious to automate the generation and use of their database by use of computers and appropriate programs because it is obvious to one of ordinary skill in the art to automate a process (see MPEP 2144.04). It would have been further obvious to add other known zinc finger proteins and their binding specificities such as the Mago zinc finger protein of Corbi

Art Unit: 1631

et al. to further increase the diversity of choices available in the database of zinc finger proteins because Choo et al.(1994b) shows on pages 642-643 that zinc finger proteins designed using fingers from the database had variability in their affinity and subsequent screening was required to select zinc finger proteins of high affinity.

8. Claims 35, 37, 38, 40, 42, 43, 48, 49, and 53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choo et al. (1994b) (Nature Vol. 372, pages 642-645, reference DB in the information disclosure statement filed 02 April 2001) in view of Choo et al. (1994a) (Proc, Natl. Acad. Sci. USA Vol. 91, pages 11163-11167, reference DD in the information disclosure statement filed 02 April 2001) in view of Isalan et al.

The claims are drawn to a method of making a zinc finger protein or a polynucleotide encoding a zinc finger protein comprising three zinc fingers that binds to a target site by using a database that comprises a plurality of precharacterized zinc finger protein sequences in which the zinc finger domains are correlated with their respective DNA binding target. In some embodiments the database comprises a zinc finger protein that has a third finger that is different from the third finger of at least one other protein in the database. In some embodiments the zinc finger proteins are designed to preserve correspondence between positions of zinc fingers in the database and the encoded protein or protein made by the method. In some embodiments the claims are drawn to computers or computer programs that execute the method, or a computer mediated method.

Choo et al. (1994b) shows a method of designing a zinc finger protein that binds to a BCR-ABL recombined oncogene target site. Choo et al. (1994b) shows on pages 642-643 that

Art Unit: 1631

each triplet of the intended binding site (shown in figure 1) was used to screen a randomized zinc finger library made by the method of Choo et al. (1994a). Selected zinc fingers that bound a desired triplet were combined into a set of three finger zinc finger proteins shown in figure 2 and further screened to select the zinc finger protein that bound the intended binding site. One zinc finger designated 1A-2A-3B was selected for expression. The expressed zinc finger protein bound the intended binding site as shown in figure 3. Choo et al. (1994b) does not explicitly show that the randomized library of zinc finger proteins consists of three finger zinc finger proteins, and further does not show the extent of precharacterization of the zinc finger proteins in the randomized zinc finger library or a database of the randomized zinc finger library. Choo et al. (1994b) does not show a computer-mediated method or computers or programs that execute the method. Choo et al. (1994b) does not show a database that comprises a zinc finger protein that has a third finger that is different from the third finger of at least one other protein in the database. Choo et al. (1994b) does not show preservation of correspondence between positions of zinc fingers in the database and the encoded protein or protein made by the method.

Choo et al. (1994a) shows on pages 11163-11164 a phage library comprising zinc finger genes in which the middle of three fingers is randomized. Choo et al. (1994a) shows on pages 11164-11166 that the library can be used to screen for members that bind the middle triplet of choice of a polynucleotide binding target. Choo et al. (1994a) shows in figure 1 the three fingers and three alternative polynucleotide binding targets. Choo et al. (1994a) shows in figure 2 a database of selected and characterized library members. Choo et al. (1994a) discusses the amino



Art Unit: 1631

acid sequence and putative secondary structures of the binding region of the selected library members.

Isalan et al. shows two variants of the zinc finger libraries of Choo et al. (1994a) in which the second and third fingers contain variant sequences on page 12027 and figure 3. The target binding site of the library members are shown in figure 3. Isalan et al. shows in the abstract and throughout that the context of neighbor fingers affects the target site specificity of a zinc finger. Isalan et al. concludes in the second column of 12027 that zinc fingers selected from a library in which two adjacent fingers are randomized allows for selection of zinc fingers with broader sequence specificity than that observed from libraries in which only one finger is randomized.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to precharacterize the selected random library members of Choo et al. (1994b) to any desired extent to aid in further analysis of selected library members because Choo et al. (1994a) shows such analysis in figure 2 and pages 11164-11167. It would have been further obvious to record such characterizations in a database as shown in Choo et al. (1994a) figure 2. It would have been further obvious to automate the generation and use of their database by use of computers and appropriate programs because it is obvious to one of ordinary skill in the art to automate a process (see MPEP 2144.04). It would have been further obvious to use libraries in which multiple fingers (including the third finger) were randomized so that zinc finger neighbor context was varied because Isalan et al. shows that randomization of neighboring fingers allows for increased diversity of binding site specificity in individual zinc fingers. It would have been further obvious to maintain correspondence between zinc finger positions in a database zinc

Art Unit: 1631

finger protein and the position of the zinc finger in a designed zinc finger because Isalan et al. shows that the identity of neighboring zinc fingers affects the binding specificity of a zinc finger.

*Allowable Subject Matter*

9. Claims 41 and 52 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

*Conclusion*

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are

Art Unit: 1631

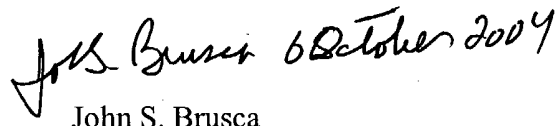
available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center at (800) 786-9199. Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward can be reached on 571 272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1631

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

 6 October 2009

John S. Brusca

Primary Examiner

Art Unit 1631

jsb